S100A6 deficiency induces senescence of mouse NIH 3T3 fibroblasts

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S100A6 (calcyclin) is a calcium binding protein of the S100 family expressed mostly in fibroblasts and epithelial cells. We have established a NIH 3T3 fibroblast cell line stably transfected with siRNA against S100A6 to examine the effect of S100A6 deficiency on non-transformed cell physiology. We report that S100A6 deficient fibroblasts reveal major phenotypic changes and proliferate at a much slower pace than control cells. Cell cycle analysis showed that a large population of these cells lost the ability to respond to serum and persisted in the G0/G1 phase. Furthermore, fibroblasts with diminished S100A6 level exhibited features of cellular senescence as revealed by β-galactosidase and gelatinase assays. Immunocytochemical examination showed changes in actin cytoskeleton and vinculin staining as well as formation of lamellipodial extensions. These features, in turn, induced a profound impact on adhesive and migratory properties of the S100A6 deficient fibroblasts. In conclusion, it appears that the S100A6 protein is indispensable for normal proliferation of mouse NIH 3T3 fibroblasts and that its deficiency may compel cells to proliferative senescence accompanied by changes in cell cytoskeleton and metabolism.